Date of Approval Letter: JUL 7 2000

FREEDOM OF INFORMATION SUMMARY

SUPPLEMENTAL NEW ANIMAL DRUG APPLICATION

NADA 141-059

CHLORMAX™ 50, CHLORMAX™ 65, or CHLORMAX™ 70 and
BMD®-25, BMD®-30, BMD®-40, BMD®-50, BMD®-60 or BMD®-75
Type A Medicated Articles

"...for the control of porcine proliferative enteropathies (PPE) associated with *Lawsonia intracellularis* susceptible to chlortetracycline and increased rate of weight gain and improved feed efficiency."

Sponsored by:
Alpharma, Inc.

NADA 141-059

FOIS-1

I. GENERAL INFORMATION

NADA Number:	141-059
Sponsor:	ALPHARMA, Inc. One Executive Drive Fort Lee, New Jersey 07024
Accepted Names:	chlortetracycline (CTC) bacitracin methylene disalicylate (BMD)
Trade Names:	CHLORMAX™ 50, CHLORMAX™ 65, or CHLORMAX™ 70 and BMD®-25, BMD®-30, BMD®-40, BMD®-50, BMD®-60 or BMD®-75 Type A Medicated Articles
Marketing Status:	Over-the-counter
Effect of Supplement:	This supplemental application adds the claim for the control of porcine proliferative enteropathies (ileitis) caused by *Lawsonia intracellularis* susceptible to chlortetracycline to approved combination label indications.

II. INDICATIONS FOR USE

A. Chlortetracycline Type A medicated articles are indicated in swine for:

1. Control of porcine proliferative enteropathies (ileitis) caused by *Lawsonia intracellularis* susceptible to chlortetracycline.

2. Treatment of bacterial enteritis caused by *Escherichia coli* and *Salmonella choleraesuis* and bacterial pneumonia caused by *Pasteurella multocida* organisms susceptible to chlortetracycline.

B. Bacitracin methylene disalicylate Type A medicated articles are indicated in growing swine for: Increased rate of weight gain and improved feed efficiency.

III. DOSAGE FORM, ROUTE OF ADMINISTRATION AND RECOMMENDED DOSAGE

A. Dosage Form: This NADA provides for the combined use of two Type A medicated articles, chlortetracycline and bacitracin methylene disalicylate, in Type B and Type C swine feeds.

B. Route of Administration: Oral, by feed

C. Recommended Dosage: In Type C medicated feed, chlortetracycline to deliver a daily dose of 10 mg/lb body weight (approximately 400 grams per ton) and 10 to 30 grams bacitracin methylene disalicylate per ton, not to exceed 14 days.

IV. EFFECTIVENESS

Data supporting the effectiveness of CTC at 10 mg/lb body weight (approximately 400 g/ton of feed) for the control of porcine proliferative enteropathies (ileitis) associated with *Lawsonia intracellularis* susceptible to chlortetracycline are in the Freedom of Information (FOI) Summary for the approval of this claim under NADA 046-699.

Data supporting the effectiveness of BMD at 10 to 30 g/ton of feed for increased rate of weight gain and improved feed efficiency in growing swine are in the FOI Summary for the approval of this claim under NADA 046-592.

The combination of CTC and BMD in swine feed is currently approved and provides appropriate concurrent use for the claims proposed. This additional claim for CTC does not overlap with those for BMD, the other drug present in this combination. Existing pharmacokinetic non-interference data in the original combination application provides substantial evidence that each of these nontopical antibacterial drugs makes a contribution to the labeled effectiveness. Accordingly, the burden to establish effectiveness of the combination use effected by this supplement has been met.

V. ANIMAL SAFETY

The target animal data upon which this application was approved are contained in the Freedom of Information (FOI) Summary for the original approval of NADA 141-059. No new data were generated for this supplemental application because the doses of CTC and BMD for this indication remain within approved ranges for swine.

VI. HUMAN FOOD SAFETY

A. *Toxicity Studies:* Data in the single ingredient applications (NADA 046-592 for BMD and NADA 046-699 for CTC) demonstrate that the use of these drugs do not constitute a hazard to human health when used in accordance with approved labeling.

B. *Acceptable Daily Intakes and Tolerances:* The Acceptable Daily Intakes (ADI) for total residues of tetracyclines, including chlortetracycline, is 25 micrograms per kilogram of body weight per day. The tolerances for the sum of tetracycline residues in uncooked edible tissues of swine are 2 ppm in muscle, 6 ppm in liver, and 12 ppm in fat and kidney (21 CFR 556.150). The tolerances for bacitracin from bacitracin methylene disalicylate are established at 0.5 ppm (0.02 unit per gram) negligible residue in uncooked edible tissues of swine (21 CFR 556.70).

C. *Tissue Residue Depletion Studies and Assay Non-Interference:* The Freedom of Information (FOI) Summary for the original approval of NADA 141-059 contains data demonstrating that the tissue concentrations of bacitracin residues are below the established tolerance at zero-day withdrawal when feed containing BMD (30 g/ton) and CTC (400 g/ton) was fed as the sole ration for 14 days. These data support the pre-slaughter withdrawal period of zero days for this drug combination.

VII. AGENCY CONCLUSIONS

The information submitted in this supplemental NADA and in the referenced files satisfies the requirements of Section 512 of the Federal Food, Drug, and Cosmetic Act, as amended by the Animal Drug Availability Act (ADAA) of 1996, and 21 CFR Part 514 of the implementing regulations. The data demonstrate that the combination of chlortetracycline and bacitracin methylene disalicylate in Type C medicated feed is safe and effective in growing swine for the uses approved in this supplemental application.

The human food safety of the single ingredients has been established under their applications as codified at 21 CFR 556.70 and 21 CFR 556.150. This combination use in swine feed does not impose an increased risk of unsafe residues.

Adequate directions for use have been written in labeling and there is reasonable certainty that pork producers will follow these directions in practice. Accordingly, the agency has concluded that this combination use shall have over-the-counter marketing status.

In accordance with 21 CFR 514.106(b)(2)(v), this is a Category II change which did not require reevaluation of safety or effectiveness data in either single-ingredient application or data in the parent combination application.

Under Section 512(c)(2)(F)(iii) of the Act, this approval for food-producing animals does not qualify for marketing exclusivity because no studies of animal safety, human food safety studies (other than bioequivalence or residue studies), or effectiveness were required for the approval of the application.

The Agency has carefully considered the potential environmental effects of this action and has concluded that the action is categorically excluded from the requirement to prepare an environmental assessment (EA) under 21 CFR 25.33(a)(2).

VIII. APPROVED PRODUCT LABELING

Copies of specimen (Blue Bird) Type B medicated feed labels are attached.

A. Blue Bird BMD3/CTC40 Type B Swine Feed

B. Blue Bird BMD1/CTC40 Type B Swine Feed

C. Blue Bird BMD/CTC Type C Swine Feed

Copies of applicable labels may be obtained by writing to the following:

Freedom of Information Office
Center for Veterinary Medicine, FDA
7500 Standish Place
Rockville, Maryland 20855